SYSTEM AND METHOD FOR HIGH NUMERIC APERTURE IMAGING SYSTEMS

CROSS-REFERENCE TO RELATED APPLICATION

This application claims the benefit of U.S. Provisional Patent Application No. 60/240,125, filed October 12, 2000, incorporated herein by reference in its entirety.

BACKGROUND OF THE INVENTION

Field of the Invention

The invention relates generally to imaging systems, and more particularly to systems and methods for high numeric aperture imaging involving low-light and high-resolution, such as used for microscopic imaging of biological samples or macroscopic imaging of astronomical samples.

Description of the Related Art

Low-light, high-resolution imaging involves situations where relatively little amount of light reflects, scatters or emanates from a target object to be viewed by using a high-resolution imaging system. Such low-light, high-resolution imaging can involve microscopic imaging of target objects including biological samples prepared using fluorescence in situ hybridization (FISH) or can involve macroscopic imaging of target objects including stars.

Conventional imaging systems are overly challenged by low-light, high-resolution imaging. Objective components used in high-resolution imaging systems need to have very high numeric aperture values. Unfortunately, a high numeric aperture value of the objective component results in a very small depth of field in which to view target objects. Small depth of field raises significant challenges in achieving and maintaining focus of target objects to be viewed during low-light, high-resolution imaging. If focus of a target object is not achieved and maintained, the resultant defocused image of the target object at a detector is spread over an unacceptably large area of the detector with a loss in

spatial resolution and decrease in signal-to-noise ratio associated with the image of the target object.

Some of the target objects involved with low-light, high-resolution imaging further challenge focusing capabilities of conventional high-resolution imaging systems. Study of these target objects requires capture of three-dimensional aspects associated with the target objects. For instance, FISH probes, having as little as 10,000 fluorescing molecules, are used to determine the presence of various chromosomes in biological cells. The FISH probes are located in three-dimensional space within the nucleus of the cell and can be oriented along the optic axis of the high-resolution imaging system. With the high sensitivity to focus in conventional high-resolution imaging systems resulting from use of high numeric aperture objective components, light from a small point source, such as a FISH probe, is easily defocused and spread out over a large area of an associated detector. If two FISH probes at the same level of defocus are imaged together, their detected images become indistinguishable from one another due to overlapping of the blurred defocused FISH probe images.

Conventional attempts to remedy focus problems involved with high-resolution imaging with high numeric aperture objective components have been only partially successful. For instance, some high-resolution imaging systems pan through the target object along the imaging system optic axis to acquire multiple image planes of the target object. These multiple image planes are then analyzed to discriminate the presence of more than one target object, such as more than one FISH probe. Unfortunately, the significant amount of time required to collect and analyze the multiple images, greatly limits the application of this approach. For example, this approach would not be readily applied to low-light, high-resolution imaging of particles or cells moving in a continuous flow past the high-resolution imaging system. Other conventional attempts include simultaneously viewing a target object from orthogonal directions, from opposite directions, or from views defined by a strobe light. Shortcomings of these conventional attempts include low throughput, poor resolution, lack of same plane object discrimination, and object positioning difficulties.

Herein are described low-light, high-resolution imaging systems and methods directed toward these and other issues. Other features and advantages will become apparent from the following detailed description, taken in conjunction with the accompanying drawings.

SUMMARY OF THE INVENTION

A system and method for high numeric aperature imaging systems includes aspects directed to a first beam splitter configured to substantially transmit part of received light as first transmitted light and to substantially reflect part of received light as first reflected light. Further aspects include a defocus system configured to modify optical power of substantially one of the following: the first transmitted light and the first reflected light, and to transmit the same as first transmitted defocused light. Additional aspects include a reflector configured to reflect one of the following: the first reflected light and the first transmitted defocused light. Further aspects include a second beam splitter configured to substantially transmit part of one of the following: the first transmitted light as second transmitted light and the first transmitted defocused light as second transmitted defocused light and configured to substantially reflect part of one of the following: the first transmitted defocused light as second reflected defocused light and the first reflected light as second reflected light.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 is a flowchart illustrating a method for augmenting depth of field at a target object for low-light, high-resolution imaging.

Figures 2-3 are schematics illustrating an imaging system for low-light, high-resolution imaging.

Figure 4-5 are schematics illustrating object planes associated with the imaging system, as shown in Figures 2-3.

Figure 6-9 are schematics illustrating alternative implementations of the imaging system, as shown in Figures 2-3.